Supplementary table 1: Definitions of outcomes from each trial

	Death	AIDS-defining events	Immune Reconstitution Inflammatory Syndrome	Serious adverse events	Loss to follow-up	Viral load suppression	ART switch
Shao et al, 2009 (THIRST)	All-cause mortality at one year [1]	Not specifically defined [2]	"a) new persistent fevers (temperature >101.5°F) developing after the initiation of ART, and not believed to be associated with ART and without an identifiable source, b) marked worsening or emergence of intrathoracic lymphadenopathy, pulmonary infiltrates or pleural effusions on radiologic examination, or c) worsening or emergence of lymphadenopathy on serial examinations or worsening of other tuberculous lesions." Up to week 104.	"Any untoward medical occurrence that resulted in death, was considered life-threatening, required inpatient hospitalization or prolongation of existing hospitalization beyond what was required in the study, or resulted in persistent or resulted in significant disability/incapacity." Up to week 104. Number of events (not number of participants with ≥1 event). Includes AIDS-defining events.	Not specifically defined, outcomes of all participants ascertained at week 104.	HIV-1 RNA <400 copies/ml at 48 weeks [3]	Not specifically defined, reported up to week 48
Abdool Karim et al 2010, 2011 (SAPiT)	All-cause mortality at 18 months	"AIDS-defining illness"	All cases of IRIS identified during the trial were retrospectively assessed and were found to meet the 2008 IRIS definition of one major or two minor clinical criteria (Meintjes et al) [27]	Grade 3-4 non-IRIS adverse events by 18 months. Number of participants with ≥1 event reported in main paper. Includes AIDS-defining illnesses.	No visit within 4 months or requested withdrawal, relocated or were unable to comply with study protocol	HIV-1 RNA <400 copies/mL at 12 months	NA
Havlir et al (STRIDE) 2011	All-cause mortality by 48 weeks	"An independent reviewer who was unaware of the study group assignment assessed new AIDS-defining events on the basis of the standardized definitions of the AIDS Clinical Trail Group."	"A reviewer who was unaware of the study-group assignments confirmed tuberculosis-associated IRIS cases on the basis of at least one major or two minor clinical criteria (Meintjes et al 2008). [27] Concurrent ART was not required for a patient to be classified as having tuberculosis-associated IRIS."	"Adverse events were graded with the use of the DAIDS Table for Grading the Severity of Adult and Paediatric Adverse events". Up to 48 weeks. Number of participants with ≥1 event.	Not specifically defined, reported up to 48 weeks.	HIV-1 RNA <400 copies/mL at 48 weeks	Not specifically defined, reported up to 48 weeks.
Blanc et al 2011	All-cause mortality	NA	"Worsening or emergence of TB symptoms after the initiation of ART in any patient who had no evidence of newly acquired infection, evolution or	Drug-related Grade 3 & 4 adverse events using DAIDS table. Up until 50 weeks after last participant was	Not specifically defined,	HIV-1 RNA <400 copies/mL	NA

(CAMELIA)	up to week 50		drug resistant TB, infection with a previously recognized pathogen, or side effects of ART. The adjudication of IRIS was not blinded"	enrolled (median 25 months). Numbers of events (not number of participants with ≥1 event). Death not specifically an SAE, although some of drug-related SAEs did lead to death.	extracted from KM graph up to week 50. [4]	at 50 weeks.	
Manosuthi et al. 2012 (TIME)	All case mortality at 1 year	"Major opportunistic infections and / or AIDS related malignancy"	"Patients were classified as having definite TB IRIS if they met criteria from a case definitions previously described by the International Network for the Study of HIV-associated IRIS" (Meintjes et al 2008). [27]	"Adverse events <u>related to ART and anti-TB drug</u>s were graded using division of AIDS table for grading of severity of adult and paediatric adverse events. Up to 96 weeks. Number of events (not number of participant with ≥1 event)."	Not defined, appears no participants LTFU.	NA	NA
Sinha et al 2012	All cause morality at 12 months.	"WHO Stage 4 event"	Not specifically defined [5]	Results section reports incidence of IRIS and "other adverse events". Not specifically defined.	Not specifically defined.	HIV-1 RNA <10,000 copies / mL at any time after 6 months on ART.	Not specifically defined.
Mfinanga et al TB-HAART	All-cause mortality at 12 months.	"Rates of other opportunistic infections (as defined according to WHO staging system) and any event which leads to progression in WHO-defined clinical staging (e.g. extrapulmonary TB) over the course of 24 months."	We used criteria from the International Network for the Study of HIV-associated Immune Reconstitution Inflammatory Syndrome for classification of tuberculosis immune reconstitution inflammatory syndrome. (Meintjes et al). As investigators, pharmacists and nurses were blinded until 6 months, presumably adjudication IRIS made without reference to ART status.	"Grade 3 and grade 4 drug related adverse events" up until 12 months. Includes IRIS as an adverse event. Number of events and numbers of people with >=1 event. No denominator of person-time provided.	Not specifically defined [6]	NA	NA [7]
Amogne et al (2015)	All cause mortality by 48 weeks.	"Category C disease listed by the CDC and WHO stage IV events"	"For the diagnosis of TB-associated IRIS, a case definition for use in resource limited settings was applied where at least one major criteria or two minor clinical criteria were required (Meintjes et al 2008).	Hepatotoxicity was graded using DAIDS table. **NB. Only refers to hepatoxicity.**	"Lost to follow-up is defined as can't be reached of outcome traced"	HIV-1 RNA <400 copies/mL at 28 weeks.	NA

Merle et al 2020 (RAFA)	All cause morality at 12 months	NA	"TB IRIS as per Meintjes et al."	Number of events (not number of participants with ≥1 event). Death included as an SAE. Full details of SAEs not available at time of writing this report [8]	Not specifically defined [8]	HIV-1 RNA < 1000 copies /mL at 18 months [9]	NA

ART: antiretroviral therapy**. IRIS:** Immune Reconstitution Inflammatory Syndrome. **TB:** tuberculosis. **NA:** not applicable. **DAIDS:** Division of AIDS Table for Grading of Severity of Adult and Paediatric Adverse Events.

(1) Three deaths occurred in study, at week 4, week 20 and week 35. No further deaths occurred in 104 weeks of follow-up (the study-specified secondary outcome).
(2) Definition of AIDS-defining events not given, however details of clinical diagnoses are provided - 1 case of cryptococcal meningitis, 1 of non-tuberculous mycobacteraemia, 1 of disseminated Kaposi's sarcoma.
(3) Also provides data on VL < 50 copies / mL
(4) Not just loss to follow-up, includes transfer out and withdrawl of consent. Overall, 12 people withdrew consent, 4 transferred HIV care and 12 were lost to follow-up over the entire course of study. Can extract from KM curve that 18 of these were before 50 weeks but not the reason for no longer being in study.
(5) IRIS isn't defined, although authors' report "all cases of IRIS were moderate and none required any interruption of HAART or management with steroids".
(6) The authors give a clear definition for ART default ("missing two consecutive monthly ART refills") which is relatively common (135 participants). Loss to follow-up not clearly defined, but they report number of people missing from final analysis (15 participants).
(7) No reported switching, ART default is reported and is defined as two or more consecutive missed monthly pick up of ART.
(8) SAE definitions not specifically defined in manuscript, protocol not available to us as we are preparing this report but will be an appendix once paper published.

Note that only a relatively small proportion of the participants had viral load measured (121 with viral load measured, at 18 months). Data also available on viral supression at 6 months (137 participants)

Supplementary table 2A: Outcomes per study (all CD4 counts)

Paper	Year pub	CD4	TB type	Early ART	Late ART	N randomised		N with mortality outcome		Death		IRIS		AIDS-defining events	
						Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
Shao (THIRST)	2009	<1200 TLC	Smear pos, any site (except CNS)	2 weeks	8 weeks	35	35	35	35	2 / 35 (6%)	1 / 35 (3%)	0 / 35 (0%)	0 / 35 (0%)	1 / 35 (3%)	2 / 35 (6%)
Abdool Karim (SAPiT)	2011	< 500	Smear pos PTB	<4 weeks	26+ weeks	214	215	188	181	15 / 188 (8%)	15 / 181 (8%)	43 / 214 (20%)	18 / 215 (8%)	18 / 214 (8%)	19 / 181 (9%)
Havlir (STRIDE)	2011	<250	Probable or confirmed, any site	2 weeks	8 - 12 weeks	405	401	368	376	31 / 368 (8%)	37 / 376 (10%)	43 / 405 (11%)	19 / 401 (5%)	26 / 405 (6%)	37 / 376 (9%)
Blanc (CAMELIA)	2011	≤ 200	Smear pos, any site	2 weeks	8 weeks	332	329	324	319	46 / 324 (14%)	63 / 319 (20%)	110 / 332 (33%)	45 / 329 (14%)	NA	NA
Manosuthi (TIME)	2012	<350	Probable or confirmed, any site	4 weeks	12 weeks	79	77	79	77	6 / 79 (8%)	5 / 77 (6%)	26 / 79 (33%)	15 / 77 (19%)	9 / 79 (11%)	14 / 77 (18%)
Sinha	2012	Any	Probable or confirmed, any site	2 - 4 weeks	8 - 12 weeks	92	89	88	62	9 / 88 (10%)	7 / 62 (11%)	9 / 92 (10%)	6 / 89 (7%)	0 / 92 (0%)	1 / 62 (1%)
Mfinanga (TB-HAART)	2014	≥ 220	Smear and culture positive PTB	2 weeks	6 months	767	771	758	765	19 / 758 (3%)	21 / 765 (3%)	81 / 767 (11%)	93 / 771 (12%)	NA	NA
Amogne 1vs4and8	2015	<200	Probable or confirmed, any site (except CNS)	1 week	4 weeks or 8 weeks	163	315	137	270	27 / 137 (20%)	37 / 270 (14%)	16 / 163 (10%)	6 / 315 (2%)	12 / 163 (7%)	27 / 270 (9%)
Amogne 1and4vs8	2015	<200	Probable or confirmed, any site (except CNS)	1 week or 4 weeks	8 weeks	323	155	273	134	47 / 273 (17%)	17 / 134 (13%)	22 / 323 (7%)	0 / 155 (0%)	26 / 323 (8%)	13 / 134 (8%)
Merle (RAFA)	Unpublished	> 50	Micro confirmed pulmonary TB	2 weeks	8 weeks	251	247	236	238	26 / 236 (11%)	35 / 238 (15%)	10 / 251 (4%)	5 / 247 (2%)	NA	NA

Paper	Serious Adverse Events (SAEs) (all)		Treatment-related SAEs / person-months		Loss to follow-up		Achieved HIV viral suppression		ART switched / discontinued	
	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
Shao (THIRST)	12 / 35 (34%)	7 / 35 (20%)	NA	NA	0 / 35 (0%)	0 / 35 (0%)	24 / 33 (73%)	19 / 34 (54%)	5 / 35 (14%)	2 / 35 (6%)
Abdool Karim (SAPiT)	112 / 214 (52%)	107 / 215 (50%)	NA	NA	46 / 214 (21%)	57 / 215 (27%)	147 / 159 (92%)	130 / 147 (88%)	16 / 214 (7%)	10 / 215 (5%)
Havlir (STRIDE)	177 / 405 (44%)	190 / 401 (47%)	NA	NA	37 / 405 (9%)	25 / 401 (6%)	293 / 331 (89%)	301 / 332 (91%)	14 / 405 (3%)	7 / 401 (2%)
Blanc (CAMELIA)	251 / 332 (76%)	245 / 329 (74%)	251 / 8567 (76%)	245 / 7632 (74%)	6 / 332 (2%)	6 / 329 (2%)	263 / 273 (96%)	238 / 247 (96%)	NA	NA
Manosuthi (TIME)	19 / 79 (24%)	19 / 77 (25%)	19 / 79 (24%)	19 / 77 (25%)	NA	NA	NA	NA	NA	NA
Sinha	21 / 92 (23%)	14 / 89 (16%)	NA	NA	15 / 92 (16%)	28 / 89 (31%)	NA	NA	4 / 92 (4%)	3 / 89 (3%)
Mfinanga (TB-HAART)	149 / 767 (19%)	174 / 771 (23%)	NA	NA	9 / 767 (1%)	6 / 771 (1%)	NA	NA	NA	NA
Amogne 1vs4and8	27 / 163 (17%)	44 / 315 (14%)	27 / 1296 (17%)	44 / 2780 (14%)	26 / 163 (16%)	45 / 315 (14%)	50 / 53 (94%)	150 / 167 (90%)	NA	NA

Paper	Serious Adverse Events (SAEs) (all)		Treatment-related SAEs / person-months		Loss to follow-up		Achieved HIV viral suppression		ART switched / discontinued	
	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
Amogne 1and4vs8	50 / 323 (15%)	21 / 155 (14%)	50 / 2676 (15%)	21 / 1400 (14%)	50 / 323 (15%)	21 / 155 (14%)	117 / 127 (92%)	83 / 93 (89%)	NA	NA
Merle (RAFA)	22 / 251 (9%)	14 / 247 (6%)	NA	NA	15 / 251 (6%)	9 / 247 (4%)	54 / 72 (75%)	38 / 49 (78%)	NA	NA

Supplementary table 2B: Outcomes per study (CD <=50)

Paper	Year pub	CD4 subgroup	TB type	Early ART	Late ART	N randomised		N with mortality outcome		Death		IRIS		AIDS-defining events	
						Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
Abdool Karim (SAPiT)	2011	< 50	Smear pos PTB	<4 weeks	26+ weeks	37	35	37	35	3 / 37 (8%)	7 / 35 (20%)	14 / 37 (38%)	4 / 35 (11%)	4 / 37 (11%)	10 / 35 (29%)
Havlir (STRIDE)	2011	< 50	Probable or confirmed, any site	2 weeks	8 - 12 weeks	144	141	NA	NA	14 / 144 (10%)	24 / 141 (17%)	26 / 144 (18%)	7 / 141 (5%)	11 / 144 (8%)	23 / NA (16%)
Blanc (CAMELIA)	2011	<= 50	Smear pos, any site	2 weeks	8 weeks	237	238	NA	NA	39 / 237 (16%)	51 / 238 (21%)	82 / 237 (35%)	24 / 238 (10%)	NA	NA
Manosuthi (TIME)	2012	< 50	Probable or confirmed, any site	4 weeks	12 weeks	46	38	46	38	4 / 46 (9%)	5 / 38 (13%)	15 / 46 (33%)	8 / 38 (21%)	NA	NA
Amogne 1vs4and8	2015	<= 50	Probable or confirmed, any site (except CNS)	1 week	4 weeks or 8 weeks	59	89	59	89	16 / 59 (27%)	21 / 89 (24%)	16 / 59 (27%)	6 / 89 (7%)	12 / 59 (20%)	27 / 89 (30%)
Amogne 1and4vs8	2015	<= 50	Probable or confirmed, any site (except CNS)	1 week or 4 weeks	8 weeks	108	40	108	40	27 / 108 (25%)	10 / 40 (25%)	22 / 108 (20%)	0 / 40 (0%)	26 / 108 (24%)	13 / 40 (32%)

Paper	Serious Adverse Events (SAEs) (all)		Treatment-related SAEs / person-months		Loss to follow-up		Achieved HIV viral suppression		ART switched / discontinued	
	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
Abdool Karim (SAPiT)	NA	NA	NA	NA	NA	NA	30 / 32 (94%)	23 / 27 (85%)	NA	NA
Havlir (STRIDE)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Blanc (CAMELIA)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Manosuthi (TIME)	15 / 46 (33%)	11 / 38 (29%)	15 / 552 (33%)	11 / 456 (29%)	0 / 46 (0%)	0 / 38 (0%)	NA	NA	NA	NA
Amogne 1vs4and8	20 / 59 (34%)	12 / 89 (13%)	NA	NA	10 / 59 (17%)	12 / 89 (13%)	16 / 16 (100%)	40 / 41 (98%)	NA	NA
Amogne 1and4vs8	25 / 108 (23%)	7 / 40 (18%)	NA	NA	17 / 108 (16%)	5 / 40 (12%)	36 / 37 (97%)	20 / 20 (100%)	NA	NA

Supplementary table 2C: Outcomes per study (CD4 > 50)

Paper	Year pub	CD4	TB type	Early ART	Late ART	N randomised		N with mortality outcome		Death		IRIS		AIDS-defining events	
						Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
Abdool Karim (SAPiT)	2011	>=50	Smear pos PTB	<4 weeks	26+ weeks	177	180	177	180	12 / 177 (7%)	8 / 180 (4%)	29 / 177 (16%)	14 / 180 (8%)	14 / 177 (8%)	9 / 180 (5%)
Havlir (STRIDE)	2011	>=50	Probable or confirmed, any site	2 weeks	8 - 12 weeks	261	260	NA	NA	17 / 261 (7%)	13 / 260 (5%)	17 / 261 (7%)	12 / 260 (5%)	15 / 261 (6%)	14 / 260 (5%)
Blanc (CAMELIA)	2011	>50	Smear pos, any site	2 weeks	8 weeks	95	91	NA	NA	7 / 95 (7%)	12 / 91 (13%)	28 / 95 (29%)	11 / 91 (12%)	NA	NA
Manosuthi (TIME)	2012	>=50	Probable or confirmed, any site	4 weeks	12 weeks	33	39	33	39	2 / 33 (6%)	0 / 39 (0%)	11 / 33 (33%)	7 / 39 (18%)	NA	NA
Mfinanga (TB-HAART)	2014	All >=220	Smear and culture positive PTB	2 weeks	6 months	767	771	684	719	19 / 767 (2%)	21 / 771 (3%)	81 / 767 (11%)	93 / 771 (12%)	NA	NA
Amogne 1vs4and8	2015	>50	Probable or confirmed, any site (except CNS)	1 week	8 weeks	104	226	104	226	11 / 104 (11%)	16 / 226 (7%)	0 / 104 (0%)	0 / 226 (0%)	0 / 104 (0%)	0 / 226 (0%)
Amogne 1and4vs8	2015	>50	Probable or confirmed, any site (except CNS)	1 week or 4 weeks	8 weeks	215	115	215	115	20 / 215 (9%)	7 / 115 (6%)	0 / 215 (0%)	0 / 115 (0%)	0 / 215 (0%)	0 / 115 (0%)
Merle (RAFA)	Unpublished	All >= 50	Micro confirmed pulmonary TB	2 weeks	8 weeks	251	247	236	238	26 / 251 (10%)	35 / 247 (14%)	10 / 251 (4%)	5 / 247 (2%)	NA	NA

Paper	Serious Adverse Events (SAEs) (all)		Treatment-related SAEs / person-months		Loss to follow-up		Achieved HIV viral suppression		ART switched / discontinued	
	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
Abdool Karim (SAPiT)	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
Havlir (STRIDE)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Blanc (CAMELIA)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Manosuthi (TIME)	4 / 33 (12%)	8 / 39 (21%)	4 / 264 (12%)	8 / 468 (21%)	0 / 33 (0%)	0 / 39 (0%)	NA	NA	NA	NA
Mfinanga (TB-HAART)	149 / 767 (19%)	174 / 771 (23%)	NA	NA	83 / 767 (11%)	52 / 771 (7%)	NA	NA	NA	NA
Amogne 1vs4and8	7 / 104 (7%)	32 / 226 (14%)	NA	NA	17 / 104 (16%)	32 / 226 (14%)	34 / 37 (92%)	110 / 126 (87%)	NA	NA
Amogne 1and4vs8	25 / 215 (12%)	14 / 115 (12%)	NA	NA	35 / 215 (16%)	14 / 115 (12%)	81 / 90 (90%)	63 / 73 (86%)	NA	NA
Merle (RAFA)	22 / 251 (9%)	14 / 247 (6%)	NA	NA	15 / 251 (6%)	9 / 247 (4%)	54 / 72 (75%)	38 / 49 (78%)	NA	NA